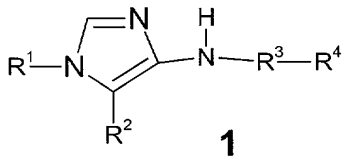
CLAIMS

What is claimed is:

1. A compound of the formula



1

wherein R^1 is a straight chain or branched (C_1-C_8)alkyl, a straight chain or branched (C_2-C_8)alkenyl, a straight chain or branched (C_2-C_8)alkynyl, (C_3-C_8)cycloalkyl, (C_4-C_8)cycloalkenyl, (3-8 membered) heterocycloalkyl, (C_5-C_{11})bicycloalkyl, (C_7-C_{11})bicycloalkenyl, (5-11 membered) heterobicycloalkyl, (C_6-C_{14}) aryl, or (5-14 membered) heteroaryl; and wherein R^1 is optionally substituted with from one to six substituents R^5 independently selected from F, Cl, Br, I, nitro, cyano, $-CF_3$, $-NR^7R^8$, $-NR^7C(=O)R^8$, $-NR^7C(=O)OR^8$, $-NR^7C(=O)NR^8R^9$, $-NR^7S(=O)_2R^8$, $-NR^7S(=O)_2NR^8R^9$, $-OR^7$, $-OC(=O)R^7$, $-OC(=O)OR^7$, $-C(=O)OR^7$, $-C(=O)R^7$, $-C(=O)NR^7R^8$, $-OC(=O)NR^7R^8$, $-OC(=O)SR^7$, $-SR^7$, $-S(=O)R^7$, $-S(=O)_2R^7$, $-S(=O)_2NR^7R^8$, $-O-S(=O)_2R^7$, $-N_3$, and R^7;

R^2 is H, F, $-CH_3$, -CN, or $-C(=O)OR^7$;

R^3 is $-C(=O)NR^9-$, $-C(=O)O-$, $-C(=O)(CR^{10}R^{11})_n-$, or $-(CR^{10}R^{11})_n-$;

R^4 is a straight chain or a branched (C_1-C_8)alkyl, a straight chain or a branched (C_2-C_8)alkenyl, a straight chain or branched (C_2-C_8 alkynyl), (C_3-C_8)cycloalkyl, (C_4-C_8)cycloalkenyl, (3-8 membered) heterocycloalkyl, (C_5-C_{11})bicycloalkyl, (C_7-C_{11})bicycloalkenyl, (5-11 membered) heterobicycloalkyl, (C_6-C_{14})aryl, or (5-14 membered) heteroaryl; and wherein R^4 is optionally substituted with from one to three substitutents R^6 independently selected from F, Cl, Br, I, nitro, cyano, $-CF_3$, $-NR^7R^8$, $-NR^7C(=O)R^8$, $-NR^7C(=O)OR^8$, $-NR^7C(=O)NR^8R^9$, $-NR^7S(=O)_2R^8$, $-NR^7S(=O)_2NR^8R^9$, $-OR^7$, $-OC(=O)R^7$, $-OC(=O)OR^7$, $-C(=O)OR^7$, $-C(=O)R^7$, $-C(=O)NR^7R^8$, $-OC(=O)NR^7R^8$, $-OC(=O)SR^7$, $-SR^7$, $-S(=O)R^7$, $-S(=O)_2R^7$, $-S(=O)_2NR^7R^8$, or R^7;

each R^7, R^8, and R^9 is independently selected from H, straight chain or branched (C_1-C_8)alkyl, straight chain or branched (C_2-C_8)alkenyl, straight chain or branched (C_2-C_8 alkynyl), (C_3-C_8)cycloalkyl, (C_4-C_8)cycloalkenyl, (3-8 membered) heterocycloalkyl, (C_5-C_{11})bicycloalkyl, (C_7-C_{11})bicycloalkenyl, (5-11 membered) heterobicycloalkyl, (C_6-C_{14})aryl, and (5-14 membered) heteroaryl, wherein R^7, R^8, and R^9 are each independently optionally substituted with from one to six substituents independently selected from F, Cl, Br, I, NO_2, -CN, $-CF_3$, $-NR^{10}R^{11}$, $-NR^{10}C(=O)R^{11}$, $-NR^{10}C(=O)OR^{11}$, $-NR^{10}C(=O)NR^{11}R^{12}$, $-NR^{10}S(=O)_2R^{11}$, $-NR^{10}S(=O)_2NR^{11}R^{12}$,

$-OR^{10}$, $-OC(=O)R^{10}$, $-OC(=O)OR^{10}$, $-OC(=O)NR^{10}R^{11}$, $-OC(=O)SR^{10}$, $-SR^{10}$, $-S(=O)R^{10}$, $-S(=O)_2R^{10}$, $-S(=O)_2NR^{10}R^{11}$, $-C(=O)R^{10}$, $-C(=O)OR^{10}$, $-C(=O)NR^{10}R^{11}$, and R^{10};

or, when R^7 and R^8 are as in NR^7R^8, they may instead optionally be connected to form with the nitrogen of NR^7R^8 to which they are attached a heterocycloalkyl moiety of from three to seven ring members, said heterocycloalkyl moiety optionally comprising one or two further heteroatoms independently selected from N, O, and S;

each R^{10}, R^{11}, and R^{12} is independently selected from H, straight chain or branched (C_1-C_8)alkyl, straight chain or branched (C_2-C_8)alkenyl, straight chain or branched (C_2-C_8 alkynyl), (C_3-C_8)cycloalkyl, (C_4-C_8)cycloalkenyl, (3-8 membered) heterocycloalkyl, (C_5-C_{11})bicycloalkyl, (C_7-C_{11})bicycloalkenyl, (5-11 membered) heterobicycloalkyl, (C_6-C_{14})aryl, and (5-14 membered) heteroaryl, wherein R^{10}, R^{11}, and R^{12} are each independently optionally substituted with from one to six substituents independently selected from F, Cl, Br, I, $-NO_2$, -CN, $-CF_3$, $-NR^{13}R^{14}$, $-NR^{13}C(=O)R^{14}$, $-NR^{13}C(=O)OR^{14}$, $-NR^{13}C(=O)NR^{14}R^{15}$, $-NR^{13}S(=O)_2R^{14}$, $-NR^{13}S(=O)_2NR^{14}R^{15}$, $-OR^{13}$, $-OC(=O)R^{13}$, $-OC(=O)OR^{13}$, $-OC(=O)NR^{13}R^{14}$, $-OC(=O)SR^{13}$, $-SR^{13}$, $-S(=O)R^{13}$, $-S(=O)_2R^{13}$, $-S(=O)_2NR^{13}R^{14}$, $-C(=O)R^{13}$, $-C(=O)OR^{13}$, $-C(=O)NR^{13}R^{14}$, and R^{13};

each R^{13}, R^{14}, and R^{15} is independently selected from H, straight chain or branched (C_1-C_8)alkyl, straight chain or branched (C_2-C_8)alkenyl, straight chain or branched (C_2-C_8 alkynyl), (C_3-C_8)cycloalkyl, (C_4-C_8)cycloalkenyl, (3-8 membered) heterocycloalkyl, (C_5-C_{11})bicycloalkyl, (C_7-C_{11})bicycloalkenyl, (5-11 membered) heterobicycloalkyl, (C_6-C_{14})aryl, and (5-14 membered) heteroaryl, wherein R^{13}, R^{14}, and R^{15} are each independently optionally substituted with from one to six substituents independently selected from F, Cl, Br, I, $-NO_2$, -CN, $-CF_3$, $-NR^{16}R^{17}$, $-NR^{16}C(=O)R^{17}$, $-NR^{16}C(=O)OR^{17}$, $-NR^{16}C(=O)NR^{17}R^{18}$, $-NR^{16}S(=O)_2R^{17}$, $-NR^{16}S(=O)_2NR^{17}R^{18}$, $-OR^{16}$, $-OC(=O)R^{16}$, $-OC(=O)OR^{16}$, $-OC(=O)NR^{16}R^{17}$, $-OC(=O)SR^{16}$, $-SR^{16}$, $-S(=O)R^{16}$, $-S(=O)_2R^{16}$, $-S(=O)_2NR^{16}R^{17}$, $-C(=O)R^{16}$, $-C(=O)OR^{16}$, $-C(=O)NR^{16}R^{17}$, and R^{16};

each R^{16}, R^{17}, and R^{18} is independently selected from H, straight chain or branched (C_1-C_8)alkyl, straight chain or branched (C_2-C_8)alkenyl, straight chain or branched (C_2-C_8 alkynyl), (C_3-C_8)cycloalkyl, (C_4-C_8)cycloalkenyl, (3-8 membered) heterocycloalkyl, (C_5-C_{11})bicycloalkyl, (C_7-C_{11})bicycloalkenyl, (5-11 membered) heterobicycloalkyl, (C_6-C_{13})aryl, and (5-12 membered) heteroaryl;

n is 0, 1, 2, or 3;

wherein R^{10} and R^{11} in $-C(=O)(CR^{10}R^{11})_n-$ and $-(CR^{10}R^{11})_n-$ are for each iteration of n defined independently as recited above;

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1, wherein R^3 is -C(=O)NH- or $-C(=O)(CR^{10}R^{11})_n-$.

3. A compound according to claim 2, wherein R^{10} and R^{11} are at each iteration of n both hydrogen.

4. A compound according to claim 1, wherein R^1 is optionally substituted (C_3-C_8)cycloalkyl or optionally substituted (C_5-C_{11}) bicycloalkyl.

5. A compound according to claim 4, wherein R^1 is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or norbornyl, each optionally substituted.

6. A compound according to claim 5, wherein R^1 is optionally substituted with from one to three substituents independently selected from F, Cl, Br, I, nitro, cyano, $-CF_3$, $-NR^7R^8$, $-NR^7C(=O)R^8$, $-OR^7$, $-C(=O)OR^7$, $-C(=O)R^7$, and R^7.

7. A compound according to claim 4, wherein R^1 is substituted with $NR^7C(=O)R^8$, (C_6-C_{14})aryl, (3-8 membered) heterocycloalkyl, or (5-14 membered) heteroaryl, and wherein said aryl, heterocycloalkyl, and heteroaryl are each optionally substituted with from one to six substituents independently selected from F, Cl, Br, I, $-NO_2$, -CN, $-CF_3$, $-NR^{10}R^{11}$, $-NR^{10}C(=O)R^{11}$, $-NR^{10}C(=O)OR^{11}$, $-NR^{10}C(=O)NR^{11}R^{12}$, $-NR^{10}S(=O)_2R^{11}$, $-NR^{10}S(=O)_2NR^{11}R^{12}$, $-OR^{10}$, $-OC(=O)R^{10}$, $-OC(=O)OR^{10}$, $-OC(=O)NR^{10}R^{11}$, $-OC(=O)SR^{10}$, $-SR^{10}$, $-S(=O)R^{10}$, $-S(=O)_2R^{10}$, $-S(=O)_2NR^{10}R^{11}$, $-C(=O)R^{10}$, $-C(=O)OR^{10}$, $-C(=O)NR^{10}R^{11}$, and R^{10}.

8. A compound according to claim 4, wherein R^1 is optionally substituted bicyclo-[3.1.0]-hexyl.

9. A compound according to claim 1, wherein R^1 is optionally substituted straight chain or branched (C_1-C_8)alkyl or optionally substituted straight chain or branched (C_2-C_8)alkenyl.

10. A compound according to claim 1, wherein R^4 is (C_6-C_{14})aryl or (5-14 membered) heteroaryl, each optionally substituted.

11. A compound according to claim 9, wherein R^4 is optionally substituted phenyl or optionally substituted pyridyl.

12. A compound according to claim 9, wherein R^4 is naphthyl, quinolyl, or isoquinolyl, each optionally substituted.

13. A compound according to claim 12, wherein R^4 is unsubstituted.

14. A compound according to claim 1, wherein R^2 is hydrogen.

15. A compound of formula 1, selected from the group consisting of:

16. A compound of claim 1, selected from the group consisting of:

N-(1-cyclobutyl-1H-imidazol-4-yl)-2-quinolin-6-yl-acetamide;

N-(1-cyclopentyl-1H-imidazol-4-yl)-2-(4-methoxy-phenyl)-acetamide;

N-[1-(*cis*-3-phenyl-cyclobutyl)-1H-imidazol-4-yl]-2-quinolin-6-yl-acetamide;

(1-cyclobutyl-1H-imidazol-4-yl)-carbamic acid phenyl ester;

1-(1-cyclobutyl-1H-imidazol-4-yl)-3-isoquinolin-5-yl-urea;

N-[1-(*cis*-3-amino-cyclobutyl)-1H-imidazol-4-yl]-2-naphthalen-1-yl-acetamide;

6-methyl-pyridine-2-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide;

1H-imidazole-4-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide;

6-hydroxy-pyridine-2-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide;

3-methyl-pyridine-2-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide;

2-pyridin-3-yl-thiazole-4-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide;

6-{*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutylcarbamoyl}-nicotinic acid methyl ester;

pyrazine-2-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide;

N-{*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-benzamide;

5-methyl-pyrazine-2-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide;

N-{*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-isobutyramide;

6-chloro-pyridine-2-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide;

quinoline-2-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide;

1H-pyrrole-2-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide;

N-{*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-2-*m*-tolyl-acetamide;

pyridine-2-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide;

2-(3-hydroxy-phenyl)-N-{*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-acetamide;

piperidine-4-carboxylic acid {*cis*-3-[4-(2-naphthalen-1-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide hydrochloride;

N-[1-(*cis*-3-acetylamino-cyclobutyl)-1H-imidazol-4-yl]-2-naphthalen-2-yl-acetamide;

N-{*cis*-3-[4-(2-isoquinolin-5-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-benzamide; and

pyridine-2-carboxylic acid {*cis*-3-[4-(2-isoquinolin-5-yl-acetylamino)-imidazol-1-yl]-cyclobutyl}-amide; and

pharmaceutically acceptable salts of the foregoing compounds.

17. A pharmaceutical composition for treating a) a disease or condition comprising abnormal cell growth; b) a neurodegenerative disease or condition; or c) a disease or condition the treatment of which can be effected or facilitated by inhibiting GSK-3, in a mammal comprising a compound of claim 1 in an amount effective intreating said disease or condition, and a pharmaceutically acceptable carrier.

18. A pharmaceutical composition for treating a disease or condition the treatment of which can be effected or facilitated by altering dopamine mediated neurotransmission in a mammal comprising a cdk5 inhibitor in an amount effective in treating said disease or condition and a pharmaceutically acceptable carrier.

19. A pharmaceutical composition according to claim 18 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically-acceptable salt thereof.

20. A pharmaceutical composition according to claim 18 wherein the disease or condition is selected from Parkinson's disease, schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, substance-induced psychotic disorder, personality disorder of the paranoid type, personality disorder of the schizoid type, drug addiction, drug withdrawal, obsessive compulsive disorder, Tourette's syndrome, depression, a mood episode, post-stroke depression, major depressive disorder, dysthymic disorder, minor depressive disorder, premenstrual dysphoric disorder, post-psychotic depressive disorder of schizophrenia, a major depressive disorder superimposed on a psychotic disorder such as delusional disorder or schizophrenia, a bipolar disorder, anxiety; attention deficit and hyperactivity disorder; and attention deficit disorder.

21. A method for treating a disease or condition comprising abnormal cell growth in a mammal comprising administering to the mammal a compound of claim 1 in an amount effective in inhibiting abnormal cell growth.

22. A method according to claim 21, wherein the disease or condition comprising abnormal cell growth is cancer.

23. A method according to claim 21, for treating a disease or condition comprising abnormal cell growth in a mammal, wherein the disease or condition is selected from benign prostate hyperplasia, familial adenomatosis polyposis, neuro-fibromatosis, atherosclerosis, pulmonary fibrosis, arthritis, psoriasis, glomerulonephritis, restenosis, hypertrophic scar formation, inflammatory bowel disease, transplantation rejection, fungal infection, and endotoxic shock.

24. A method for treating a diseases or condition comprising abnormal cell growth in a mammal comprising administering to the mammal a compound of claim 1 in an amount effective to inhibit cdk2 activity.

25. A method according to claim 24, wherein the disease or condition comprising abnormal cell growth is cancer.

26. A method according to claim 24, for treating a disease or condition comprising abnormal cell growth in a mammal, wherein the disease or condition is selected from benign prostate hyperplasia, familial adenomatosis polyposis, neuro-fibromatosis, atherosclerosis, pulmonary fibrosis, arthritis, psoriasis, glomerulonephritis, restenosis, hypertrophic scar formation, inflammatory bowel disease, transplantation rejection, fungal infection, and endotoxic shock.

27. A method for treating a neurodegenerative disease or condition in a mammal comprising administering to the mammal a compound of claim 1 in an amount effective in treating said disease or condition.

28. A method according to claim 27 wherein the neurodegenerative disease or condition is selected from Huntington's disease, stroke, spinal cord trauma, traumatic brain injury, multiinfarct dementia, epilepsy, amyotrophic lateral sclerosis, pain, viral induced dementia for example AIDS induced dementia, neurodegeneration associated with bacterial infection, migraine, hypoglycemia, urinary incontinece, brain ischemia, multiple sclerosis, Alzheimer's disease, senile dementia of the Alzheimer's type, mild cognitive impairment, age-related cognitive decline, emesis, corticobasal degeneration, dementia pugilistica, Down's syndrome, myotonic dystrophy, Niemann-Pick disease, Pick's disease, prion disease with tangles, progessive supranuclear palsy, lower lateral sclerosis, and subacute sclerosing panencephalistis.

29. A method for treating a disease or condition the treatment of which can be effected or facilitated by altering dopamine mediated neurotransmission in a mammal comprising administering to the mammal a cdk5 inhibitor in an amount effective in treating said disease or condition.

30. A method according to claim 29 wherein the disease or condition is selected from Parkinson's disease, schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, substance-induced psychotic disorder, personality disorder of the paranoid type, personality disorder of the schizoid type, drug addiction, drug withdrawal, obsessive compulsive disorder, Tourette's syndrome, depression, a mood episode, post-stroke depression, major depressive disorder, dysthymic disorder, minor depressive disorder, premenstrual dysphoric disorder, post-psychotic depressive disorder of schizophrenia, a major depressive disorder superimposed on a psychotic disorder such as delusional disorder

or schizophrenia, a bipolar disorder, anxiety; attention deficit and hyperactivity disorder; and attention deficit disorder.

31. A method according to claim 29 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically-acceptable salt thereof.

32. A method for treating in a mammal a disease or condition selected from male fertility and sperm motility; diabetes mellitus; impaired glucose tolerance; metabolic syndrome or syndrome X; polycystic ovary syndrome; adipogenesis and obesity; myogenesis and frailty, for example age-related decline in physical performance; acute sarcopenia, for example muscle atrophy and/or cachexia associated with burns, bed rest, limb immobilization, or major thoracic, abdominal, and/or orthopedic surgery; sepsis; hair loss, hair thinning, and balding; and immunodeficiency; which method comprises administering to said mammal an amount of a compound according to claim 1 effective in treating said disease or condition.

33. A method for inhibiting GSK-3 in a mammal, which method comprises administering to said mammal an amount of a compound according to claim 1 effective in inhibiting GSK-3.

34. A pharmaceutical composition for treating depression or anxiety in a mammal comprising a cdk5 inhibitor and

a) an NK-1 receptor antagonist;

b) a $5HT_{1D}$ receptor antagonist; or

c) an SSRI;

wherein the cdk5 inhibitor and a), b), or c) are together in an amount effective in treating depression or anxiety, and a pharmaceutically acceptable carrier.

35. A pharmaceutical composition according to claim 34 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.

36. A method for treating depression or anxiety in a mammal which method comprises administering to said mammal a cdk5 inhibitor and

a) an NK-1 receptor antagonist;

b) a $5HT_{1D}$ receptor antagonist; or

c) an SSRI;

wherein the combined amounts of the cdk5 inhibitor and a), b), or c) are effective in treating depression or anxiety.

37. A method according to claim 36 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.

38. A pharmaceutical composition for treating schizophrenia in a mammal comprising a cdk5 inhibitor and as antipsychotic selected from ziprasidone, olanzapine, risperidone, L-745870, sonepiprazole, RP 62203, NGD 941, balaperidone, flesinoxan, and

gepirone, together in an amount effective in treating schizophrenia, and a pharmaceutically acceptable carrier.

39. A pharmaceutical composition according to claim 38 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.

40. A method of treating schizophrenia in a mammal which method comprises administering to said mammal a cdk5 inhibitor and an antipsychotic selected from ziprasidone, olanzapine, risperidone, L-745870, sonepiprazole, RP 62203, NGD 941, balaperidone, flesinoxan, and gepirone, wherein the combined amounts of the cdk5 inhibitor and the antipsychotic are effective in treating schizophrenia.

41. A method according to claim 40 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.

42. A pharmaceutical composition for treating a disorder selected from Alzheimer's disease, mild cognitive impairment, and age-related cognitive decline in a mammal comprising a cdk5 inhibitor and an acetylcholinesterase inhibitor together in an amount effective in treating said disorder, and a pharmaceutically acceptable carrier.

43. A pharmaceutical composition according to claim 42 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.

44. A method for treating in a mammal a disorder selected from Alzheimer's disease, mild cognitive impairment, and age-related cognitive decline, which method comprises administering to said mammal a cdk5 inhibitor and an acetylcholinesterase inhibitor, wherein the combined amounts of the cdk5 inhibitor and the acetylcholinesterase inhibitor are effective in treating said disorder.

45. A method according to claim 44 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.

46. A pharmaceutical composition for treating a disease or condition selected from stroke, spinal cord trauma, traumatic brain injury, multiinfarct dementia, epilepsy, pain, Alzheimer's disease, and senile dementia in a mammal comprising a cdk5 inhibitor and

a) TPA; or

b) NIF;

wherein the cdk5 inhibitor and TPA or NIF are together in an amount effective in treating said disorder, and a pharmaceutically acceptable carrier.

47. A pharmaceutical composition according to claim 46 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.

48. A method for treating in a mammal a disease or condition selected from stroke, spinal cord trauma, traumatic brain injury, multiinfarct dementia, epilepsy, pain,

Alzheimer's disease, and senile dementia, which method comprises administering to said mammal a cdk5 inhibitor and

a) TPA; or

b) NIF;

wherein the combined amounts of the cdk5 inhibitor and TPA or NIF are effective in treating said disease or condition.

49. A method according to claim 48, wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.

50. A pharmaceutical composition for treating a disease or condition selected from Huntington's disease, stroke, spinal cord trauma, traumatic brain injury, multiinfarct dementia, epilepsy, amyotrophic lateral sclerosis, pain, viral induced dementia for example AIDS induced dementia, migraine, hypoglycemia, urinary incontinece, brain ischemia, multiple sclerosis, Alzheimer's disease, senile dementia of the Alzheimer's type, mild cognitive impairment, age-related cognitive decline, emesis, corticobasal degeneration, dementia pugilistica, Down's syndrome, myotonic dystrophy, Niemann-Pick disease, Pick's disease, prion disease with tangles, progessive supranuclear palsy, lower lateral sclerosis, and subacute sclerosing panencephalistis in a mammal comprising a cdk5 inhibitor and an NMDA receptor antagonist together in an amount effective in treating said disorder, and a pharmaceutically acceptable carrier.

51. A pharmaceutical composition according to claim 50 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.

52. A method for treating in a mammal a disease or condition selected from Huntington's disease, stroke, spinal cord trauma, traumatic brain injury, multiinfarct dementia, epilepsy, amyotrophic lateral sclerosis, pain, viral induced dementia for example AIDS induced dementia, migraine, hypoglycemia, urinary incontinece, brain ischemia, multiple sclerosis, Alzheimer's disease, senile dementia of the Alzheimer's type, mild cognitive impairment, age-related cognitive decline, emesis, corticobasal degeneration, dementia pugilistica, Down's syndrome, myotonic dystrophy, Niemann-Pick disease, Pick's disease, prion disease with tangles, progessive supranuclear palsy, lower lateral sclerosis, and subacute sclerosing panencephalistis, which method comprises administering to said mammal a cdk5 inhibitor and an NMDA receptor antagonist, wherein the combined amounts of the cdk5 inhibitor and the NMDA receptor antagonist are effective in treating said disease or condition.

53. A method according to claim 52 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.

54. A pharmaceutical composition for treating a disease or condition selected from stroke, spinal cord trauma, traumatic brain injury, multiinfarct dementia, epilepsy, pain, Alzheimer's disease, and senile dementia in a mammal comprising a cdk5 inhibitor and a potassium channel modulator together in an amount effective in treating said disorder, and a pharmaceutically acceptable carrier.

55. A pharmaceutical composition according to claim 54 wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.

56. A method for treating in a mammal a disease or condition selected from stroke, spinal cord trauma, traumatic brain injury, multiinfarct dementia, epilepsy, pain, Alzheimer's disease, and senile dementia, which method comprises administering to said mammal a cdk5 inhibitor and a potassium channel modulator, wherein the combined amounts of the cdk5 inhibitor and the potassium channel modulator are effective in treating said disease or condition.

57. A method according to claim 56, wherein the cdk5 inhibitor is a compound of formula 1 or a pharmaceutically acceptable salt thereof.